

Oxygen consumption measurements were made in an Oxymax chamber with an air flow rate of 0.18l/min for 2 hr at 25°C. Airflow was controlled and measured using a mass flow meter (Flow control [R-1], Applied Electrochemical Inc., Pittsburgh, PA). Gas composition of incoming outdoor air and exhaust gas were measured using an infrared gas analyzer for CO₂ (Infrared Analyzer 864, Beckman Instruments, Fullerton, CA), and an electrochemical O₂ detector (Ametek S-3A, Applied Electrochemical Inc., Pittsburgh, PA). Gas analyzers were calibrated daily using cylinders of primary gas standard mixtures with known concentrations of CO₂, O₂ and N₂. Each animal was placed in a respiration chamber and was allowed to equilibrate for 1 hr. Oxygen consumption and CO₂ production were monitored every 5 min during the 2nd hr with the use of a computer-controlled open circuit calorimetry system. Values for energy expenditure (Elia and Livesey, 1992) were calculated every 5 min. Instruments were interfaced with a computer for calculations.

As expected, *ob/ob* mice were significantly hypothermic ($35.6 \pm 0.2^\circ\text{C}$) compared to their lean littermates ($36.9 \pm 0.2^\circ\text{C}$, $P < 0.01$). After 12-day treatment with 150 mg/kg extract, body temperature in *ob/ob* mice significantly increased from $35.6 \pm 0.1^\circ\text{C}$ (Day 0) to $36.6 \pm 0.1^\circ\text{C}$ (Day 12, $P < 0.01$).

Energy expenditure values were obtained in *ob/ob* mice treated with vehicle or *Panax ginseng* extract 150 mg/kg (FIG. 22). After the 12-day treatment, there was a significant increase in energy expenditure of the extract-treated group compared to the vehicle-treated group (19.3 ± 1.0 cal/min vs. 12.6 ± 0.4 cal/min, $P < 0.01$).

EXAMPLE 15

PLASMA CHOLESTEROL CHANGES

Panax ginseng berry extract also significantly reduced plasma cholesterol levels in *ob/ob* mice (FIG. 23). Plasma cholesterol concentration of 150 mg/kg extract-treated *ob/ob* mice was significantly lower (117 ± 18.3 mg/dl) compared to the vehicle-treated animals (169 ± 12.4 mg/dl, $P < 0.05$).

EXAMPLE 16

METABOLIC PARAMETERS

Additional metabolic parameters are measured using techniques well known in the art. For example, analysis of biochemical parameters, such as, insulin, triglyceride, cholesterol, free fatty acids, and glycerol are performed spectrophotometrically on a clinical chemistry analyzer. Insulin is measured by radioimmunoassay (Cambridge Diagnostics, Billerica, MA).

EXAMPLE 17

GINSENG BERRY FRACTIONS AND BLOOD GLUCOSE

For studies with fractions, oral administration (3, 10, 30 and 100 mg/kg) is used. Troglitazone (30 mg/kg in rats; Luo *et al.*, 1998) is used as a positive control. Troglitazone is a currently used oral agent that improves peripheral insulin sensitivity.

The HPLC fractionation, purification, and quantification studies are performed as previously described in the present invention.

The effect of ginseng berry fractions on fasting blood glucose is examined in adult *ob/ob* mice, and lean C57BL/6J mice that are weight-matched and divided into 6 groups. Each group is treated with a daily oral ginseng berry fraction (50, 150 mg/kg) or vehicle for 12 days. After a 4 h fast, on day 0 (before treatment), 5, and day 12, 10 μ l blood is collected from the tail vein for measurement of fasting glucose level. Intraperitoneal glucose tolerance test (IPGTT) is done on day 0 (before treatment) and day 12 (last day of treatment). On the day of the test, animals are fasted for 4 hr (starting from 9:00AM) followed by an intraperitoneal injection of glucose (2 g/kg). Blood glucose levels are determined in blood samples from the tail vein at 0 (prior to), and 30, 60 and 120 min after glucose administration with a Glucose Analyzer (Hemocue AB, Angelholm, Sweden).

It is contemplated that some of the ginseng berry HPLC fractions will give variable effects with the fasting blood glucose test and glucose tolerance. Previous studies with type 1 diabetic mice have shown that glycan fractions of *Panax ginseng* root have significant anti-hyperglycemic activity. In type 2 diabetes models, hyperglycemia is
5 mainly due to insulin resistance, and may not be related to defects in insulin secretion (as seen in type 1 model).

EXAMPLE 18

DIABETIC PATIENTS TREATED WITH EXTRACT OR ACTIVE COMPOUND

For clinical studies, the whole berry extract, compositions comprising at least one
10 ginsenoside or compositions comprising more than one ginsenoside, and/or an organic extracts comprising at least one ginsenoside are administered to a subject suffering from hyperglycemia and/or type 2 diabetes. Ginsenosides are highly lipid soluble, thus an organic solvent can be used to solublize the ginsenosides.

Administration of the extract or active compound comprises a variety of routes
15 depending upon the form of the extract or compound. For example, whole berry extract is administered orally. Administration of the compositions comprising a single ginsenoside or compositions comprising multiple ginsenosides is administered subcutaneously. Subcutaneous administration includes, but is not limited to, a single injection, multiple injections or continuous infusion. And administration of the organic
20 extract or the compositions comprising a one or more than one ginsenoside is administered transdermally via a patch. In addition to administering the extract or the active compound, a placebo compound is administered to subjects via similar routes.

For the experiments, the subjects (diabetic) are treated with at least a daily dose of the compound or placebo for a period of time, *e.g.*, 5 days, 12 days, 14 days, 21 days or
25 longer.

The endpoint of the treatment period comprises measurement of blood glucose levels via a variety of techniques that are well known and used by clinical laboratories.